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February 8, 2008

Application No.	:	**2,375,868**
Owner	:	KYOWA MEDEX CO., LTD.
Title	:	**STABILIZED DENATURED LIPOPROTEIN AND METHOD FOR PRODUCING THEREOF**
Classification	:	C07K 14/775 (2006.01)
Your File No.	:	**883-136 MIS**
Examiner	:	R. Qanbar

YOU ARE HEREBY NOTIFIED OF A REQUISITION BY THE EXAMINER IN ACCORDANCE WITH SUBSECTION 30(2) OF THE *PATENT RULES*. IN ORDER TO AVOID ABANDONMENT UNDER PARAGRAPH 73(1)(A) OF THE *PATENT ACT*, A WRITTEN REPLY MUST BE RECEIVED WITHIN 6 MONTHS AFTER THE ABOVE DATE.

This application has been examined taking into account the:

Description,	pages 1-4, 8-53, as originally filed; pages 5-7, as received on June 2, 2005 during the national phase;
Claims,	1-21, as originally filed; and
Drawings,	pages 1/10 - 10/10, as originally filed.

This application has been examined taking into account applicant's correspondence received in this office on June 2, 2005.

The number of claims in this application is 21.

The search of the prior art has revealed the following:

References Applied:

Canadian Application 2119096 ¤	September 20, 1994	Lang, H. et al
Japanese Application 9-297137 ¤ (Machine translation)	November 18, 1997	Yamada, S. et al

Publications

Methods Enzymol	1986	128: 208-613	Kreiger, M.
(From http://www.cumc.columbia.edu/dept/medicine/tabas_site/protocols/acldl.pdf)			
J. Biochem. ¤	1987	101: 729-741	Murakami, M. et al
Clin. Chem.	1992	38: 1873-1877	Sgoutas, D.S. et al

¤ citation stemming from a foreign search report

Lang et al disclose lyophilisation as a reason for denaturation of lipoproteins (page 1, third paragraph). Also disclosed are lipoproteins lyophilised in the presence of stabilisers, such as sucrose, and the use of the lyophilised preparations as a reference for diagnostic purposes.

Yamada et al disclose the use of denatured lipoproteins as a standard for lipoprotein determinations. Disclosed methods for denaturing lipoproteins include copper oxidation (paragraphs 177-179 and Figure 3), reduction (paragraphs 197 and 198 and Figure 4), and proteolysis (paragraphs 208 and 209). The denatured lipoprotein is recognised by monoclonal antibodies raised against synthetic peptides and found to be specific to the denatured form of the lipoprotein (paragraph 154).

Kreiger discloses a form of the lipoprotein LDL, which is first denatured by acetylation, then preserved by lyophilisation.

Murakami et al disclose various methods for denaturing the lipoprotein HDL by chemical modifications. These modifications include acetylation and malondialdehyde treatment.

Sgoutas et al disclose freezing and thawing as a means of denaturing lipoprotein Lp(a).

The examiner has identified the following defects in the application:

Claims 1 and 15 do not comply with paragraph 28.2(1)(*b*) of the *Patent Act* because these claims include subject matter disclosed in Kreiger before the claim date. Described in this reference is a denatured and lyophilised lipoprotein, namely lyophilised acetylated LDL.

Claims 10 and 15 do not comply with paragraph 28.2(1)(*b*) of the *Patent Act* because these claims include subject matter disclosed individually by Sgoutas et al and Lang et al before the claim date. Each of these references describes a method of denaturing a lipoprotein and lipoprotein denatured by using this method. Sgoutas et al describes lipoprotein Lp(a) denatured as a result of freezing and thawing, while Lang et al describes lipoproteins that are denatured by the process of freeze-drying followed by reconstitution.

Claims 1, 15, 16 and 20 do not comply with section 28.3 of the *Patent Act*. The subject matter of these claims would have been obvious on the claim date to a person skilled in the art or science to which they pertain having regard to Yamada et al in view of common general knowledge (claims 1, 15, 16 and 20), exemplified by Lang et al (claims 1, 16 and 20). Yamada et al teach the use of lipoproteins denatured by various methods as reliable standards for lipoprotein determination. Lang et al describe the use of the common technique of lyophilisation as a means of preserving lipoproteins, particularly in the presence of sucrose as a stabiliser. A

skilled artisan would have had no difficulty applying the commonly used technique of lyophilisation, for example as described by Lang et al, to the denatured lipoproteins of Yamada et al, thus arriving at the subject matter of the above-mentioned claims.

Claims 1 and 15 do not comply with section 28.3 of the *Patent Act*. The subject matter of these claims would have been obvious on the claim date to a person skilled in the art or science to which they pertain having regard to Murakami et al in view of Lang et al. Murakami et al teach the denaturation of lipoproteins by chemical modification. Lang et al describe the use of lyophilisation, a technique that is well-known in the art, to stabilise lipoproteins. It would have been within the competence of a skilled artisan to lyophilise the denatured proteins of Murakami et al so as to arrive at the subject matter of the aforementioned claims.

Claim 20 is indefinite and does not comply with subsection 27(4) of the *Patent Act*. The "reagent kit" is not defined adequately. A kit contains at least two components, but only one is defined in this claim. All the essential components of the claimed kit must be defined in the claim.

Claim 21 is indefinite and does not comply with subsection 27(4) of the *Patent Act*. The inclusion of "the whole or part of stabilized denatured lipoprotein" results in a lack of clarity. The meaning of "the whole or part" relative to a stabilised denatured lipoprotein is uncertain.

Under section 76 of the *Patent Rules*, every trade-mark must be identified as a trade-mark. If "Sepharose" on page 14, line 6; "Kyowa", and "Sephadex" on page 29, lines 9 and 12; and "Sephacryl", and "Tween" on page 31, lines 9 and 31, are trade-marks, they must be so identified.

In view of the foregoing defects, the applicant is requisitioned, under subsection 30(2) of the *Patent Rules*, to amend the application in order to comply with the *Patent Act* and the *Patent Rules* or to provide arguments as to why the application does comply.

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